

IN THE SPECIFICATION:

On page 2, lines 22 to 28, please delete the paragraph and replace it with the following.

Numerous proteins have been described that interact with some specificity with an ARE, but their exact role in the process of mRNA turnover remains to be defined. For example, proteins which bind to the ARE described above include HuR and other ELAv family proteins, such as HuR (also called HuA), Hel-N1 (also called HuB), HuC and HuD; AUF 1 (four isoforms); tristetraprolin; AUH; TIA; TIAR; glyceraldehyde-3-phosphate; hnRNP C; hnRNP A1; AU-A; and AU-B. Many others have not been extensively characterized.

On page 7, line 4 to 11, please delete the paragraph and replace it with the following.

The method of the present invention is useful for identifying agents which can either increase or decrease the stability of said target RNA sequence. Such agents may be capable of modulating the activity of an RNA binding molecule such as, but not limited to, C-rich element binding proteins and AU rich element binding proteins, examples of the latter including HuR and other ELAv family proteins, such as HuR, Hel-N1, HuC and HuD; AU-1; tristetraprolin; AUH; TIA; TIAR; glyceraldehyde-3-phosphate; hnRNP C; hnRNP A1; AU-A; and AU-B. This list is provided as illustrative of the types of molecules that may be evaluated in the present invention, but is by no means limiting.

On page 8, line 1 to 13, please delete the paragraph and replace it with the following.

The non-limiting selection of the components of this method are as described above. The aforementioned method is useful, for example, when the RNA stability modifier decreases the stability of said target RNA sequence, and the agent to be identified increases the stability of the target RNA sequence that is decreased by the RNA stability modifier. In addition, the method is useful when the RNA stability modifier increases the stability of the target RNA sequence, and the agent to be identified decreases the stability of the target RNA sequence that is increased by the RNA stability modifier. Non-limiting examples of RNA stability modifiers include C-rich element binding proteins, and AU rich element binding proteins, examples of AU rich element binding proteins, including HuR and other ELAv family proteins, such as HuR, Hel-N1, HuC and HuD; AUF1; tristetraprolin; AUH; TIA; TIAR; glyceraldehyde-3-phosphate; hnRNP C; hnRNP A1; AU-A; and AU-B. This list is provided as illustrative of the types of molecules that may be evaluated in the present invention, but is by no means limiting.

Starting on page 20, line 8 and ending on page 21, line 4, please delete the paragraph and replace it with the following.

The key to the development of the system and methods utilizing the system are based on the discovery that polyadenylate competitor RNA is capable of sequestering proteins that bind polyadenylate and consequently activating the deadenylase enzyme, inducing RNA turnover. As it was heretofore considered that such proteins that bind polyadenylate may contribute to RNA deadenylation, the present finding that such proteins are, in contrast, stabilizers of RNA, led to the realization that such proteins are

interacting with and inactivating destabilizing mediators *in vivo*. Thus, the present invention is directed to an *in vitro* system capable of recapitulating regulated RNA turnover of an exogenously added preselected target RNA sequence comprising a cell extract depleted of activity of proteins that bind polyadenylate, and a preselected target RNA sequence. In one particular embodiment, the regulated RNA turnover is that modulated by AU-rich element (ARE) regulated RNA turnover. Examples of mRNAs with AU-rich elements include those of, by way of non-limiting example, c-fos; c jun; c-myc TNF- $\alpha$ , GMCSF, IL1-15, and IFN- $\beta$ . As noted above, AU-rich elements are sites for binding of numerous proteins, including the ELAV family of ARE-binding proteins, such as HuR, He1-N1, HuC and HuD; others include AUF1; tristetraprolin; AUH; TIA; TIAR; glyceraldehyde-3-phosphate; hnRNP C; hnRNP A1; AU-A; and AU-B. In another embodiment, the regulated RNA turnover is that modulated by C-rich element (CRE) regulated RNA turnover, such elements as found in the mRNA of globin mRNAs, collagen, lipoxygenase, and tyrosine hydroxylase. Another mRNA with an as yet uncharacterized sequence element is that of VEGF. The invention, however, is not so limiting as to the particular elements or binding proteins to these elements involved in the regulation of RNA turnover.